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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,331	02/22/2007	Adrienne S. Gordon	27432-16428	2103

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EXAMINER	
CORNET, JEAN P	
ART UNIT	PAPER NUMBER
1628	
MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,331	GORDON ET AL.	
	Examiner	Art Unit	
	JEAN CORNET	1628	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *21, 36, 58, 78, 86, 93, 95, 118, 119, 134, 137, 142 and 145* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 146, 148-153, 155-164* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,21,36,58,78,86,93,95,118,119,134,137,145,146,148-153 and 155-164.

DETAILED ACTION

Claims 2-20, 22-35, 37-57, 59-77, 79-58, 94, 96-117, 120-133, 135-136, 138-141, 143-144, 147 and 154 are canceled by Applicant. Claims 1, 21, 36, 58, 78, 86, 93, 95, 118, 119, 134, 137, 142, 145, 146, 148-153, 155-164 are pending. Claims 21, 36, 58, 78, 86, 93, 95, 118, 119, 134, 137, 142 and 145 are withdrawn. The amendment filed on 02/16/2010 in response to the Non-Final office Action of 11/13/2009 is acknowledged and has been entered.

Rejection remained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 155, 156, 158, 161-164 **remain** provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 6, 19-24 of copending Application No. 11/153,725.

Applicant's Arguments

Applicant's arguments that Yao et as (Cell. 109:733-743, June 2002) is not properly prior art to the instant application because Yao was published after the instant applicant's filling date , see page 10, filed 02/16/2010, with respect to rejection under 35 USC § 103 have been fully considered and are persuasive.

Response to Arguments

Yao et al reference is published after the instant application filling date so therefore Yao et al can not be considered as prior art. Therefore the 103 rejection of claims 1, 146-163 has been withdrawn. Rejections and objections not reiterated form previous Office Action are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

New Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 14 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The limitation "wherein said administering of said adenosine receptor antagonist and said dopamine receptor antagonist enhances the potency of said adenosine receptor antagonist" is unclear for what purpose the potency of one agonist (i.e. adenosine receptor antagonist) is enhanced by administering it with a dopamine receptor antagonist. Merriam-Webster dictionary defines potency as the ability or capacity to achieve or bring about a particular result. It is unclear what the particular result Applicant is trying to achieve by enhancing the potency of the adenosine receptor antagonist.

Claim Rejections - 35 USC § 103

Claims 1, 146, 148-153, 155-164 are rejected under 35 U.S.C. 103(a) as being unpatentable over Diamond et al (US5,069,895) cited in IDS in view of Koch et al. " Regulation of sensorimotor gating by interactions of dopamine and adenosine in the rat", Behavioural Pharmacology, vol. 9, no. 1, 1998 cited in IDS, Fink et al "Molecular cloning of the rat A_2 adenosine receptor: selective co-expression with D_2 dopamine receptors in rat striatum", Molecular Brain Research, vol. 14, Issue 3, July 1992, pages 186-195, Dar, "Modulation of ethanol-induced motor incoordination by mouse striatal A_1 adenosinergic receptor", Brain Research Bulletin, Vol. 55, No. 4, pp 513-520, 2001 and Beasley et al. (US6,159,963) cited in IDS.

Diamond teaches methods of treating acute, chronic ethanol dependence or withdrawal syndrome by administration of adenosine receptor antagonist to a host in an amount sufficient to reduce the symptoms of ethanol withdrawal (see claim 1 and 11). Although the standard therapeutically effective dosage for use is generally in the range from about 0.01ug/kg to 5 mg/kg as to claim 150, the amount will depend on the subject being treated, the severity and nature of the affliction, the manner of administration, the potency and pharmacodynamics of the particular agent (col. 5, ln. 11-19). The preferred adenosine antagonist is PD115199 (col. 3, lines 7-30). Lastly Diamond teaches the administration can be in a single unit dose (col. 4, lines 19-25).

Diamond does not expressly teach administration of a dopamine receptor antagonist to treat ethanol addictive behavior.

Koch et at teach the interactions between DA and adenosine A_{2A} as well as between DA D_1 and adenosine A_1 receptors A_{2A} seem to be antagonistic, which means that the stimulation of adenosine A_1 and A_{2A} receptors inhibit D_1 or D_2 receptor mediated effects, probably involving separate populations of striatal projection neurons (page 23, right col. first para). Moreover Koch et al further teaches that there is strong evidence that the physiological effects of DA in the striatum are modulated by adenosine via different types of DA and adenosine receptors (page 23, left col. second para).

Fink et al teach several lines of evidence have previously suggested that dopamine-induced changes in motor behavior can be modulated by adenosine analogs acting at the A_2 subtype of adenosine receptor in the fore brain and the co-expression of D_2 dopamine and A_2

adenosine receptors in a subset of striatal cells provides an anatomical basis for dopaminergic-adenosinergic interactions on motor behavior (abstract).

Dar teaches that striatum is an additional brain motor area involved in mediating ethanol's motor coordination and even the smallest dose of adenosine antagonist significantly attenuated ethanol-induced motor incoordination (page 518, right col). Dar further teaches A_{2A} receptors are mainly localized on the intrinsic striatal neurons and dopaminergic terminals (page 518, left col.).

Beasley teaches a method for treating substance abuse comprising administering an effective amount of olanzapine (a dopamine antagonist) to a patient in need thereof (abstract) and a method for treating adverse withdrawal syndrome said substance abuse include opiods, cocaine, anxiolytic and hypnotic drugs, and alcohol (col. 1, lines 65-67; col, 2, lines 1-3) and adverse withdrawal syndrome refers to an adverse condition resulting form the cessation or withdrawal from substance abuse (col. 5, lines 25-28). For the treatment of alcohol abuse, a lower dosage may be appropriate than treatment than the preferred standard effective dose of 1mg to 25mg per day (col 7, lines 35-45).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to administer an adenosine antagonist with an dopamine antagonist sequentially or simultaneously recited in claims 160 and 161 to mitigate one or more symptoms associated with chronic consumption of a substance abuse by administration of adenosine receptor antagonist and dopamine receptor antagonist . One or ordinary skill in the art would have been motivated to do so because the beneficial synergistic effect of adenosine A2 and dopamine D2 receptors has been fully envisaged at the time of filling, since Koch et at teach the

interactions between DA and adenosine A_{2A} as well as between DA D_1 and adenosine A_1 receptors A_{2A} seem to be antagonistic and Fink et al teach the co-expression of D_2 dopamine and A_2 adenosine receptors in a subset of striatal cells provides an anatomical basis for dopaminergic-adenosinergic interactions on motor behavior.

One skill in the art would have been motivated to administer the combined D2 and A2 antagonists to mitigate one or more symptoms associated with chronic consumption of alcohol because each of the therapeutics agents with an effective dose had been individually taught in the prior art to be successful at treating substance abuse. The instant situation is amenable to the type of analysis set forth *in re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions that is taught by the prior art to be useful for the same purpose in order for a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Applying the same logic to the instant process claims, one of ordinary skill in the art would have had reasonable expectation of success that by administering an effective dose of adenosine receptor antagonist taught by Diamond et al in combination with an effective dose of dopamine receptor antagonist taught by Beasley et al, one would achieve a method of treating one or more symptoms associated with chronic consumption of a substance abuse.

With respect to claims 149, 150, 152, 153, even though the references are silent as to administration of a standard, sub-threshold, and a threshold dosage, It would have been prima facie obvious to one of ordinary skill in the art to combine the teaching of Diamond and Beasley to optimize via routine experimentation the dosage range recited in Diamond and Beasley because Diamond suggests the amount PD 115,199 depends on the subject being treated, the

severity and nature of the affliction, the manner of administration, the potency and pharmacodynamics of the particular agent and Beasley suggests a lower dose than the standard dose for the treatment of alcohol, thus resulting in the practice of the instantly claimed invention.

MPEP 2144.5(A) states:

Optimization Within Prior Art Conditions or Through Routine Experimentation

> Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)

One would have been motivated to do so; with reasonable expectation of success because such optimization is routine in the pharmaceutical and would have been readily accomplished by one of ordinary skill in the art without undue burden. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

With respect to claims 156, 157, 159, 160, one would have recognized lowering the dosage of these agents would reduce the side effects caused by these agents. The side effects recited in these claims are well known because these compounds are well known in the art and efficacy and toxicity have already been proven. These minor differences found adverse symptoms does not render the claims patentable distinct because the techniques and skills for

determining efficacy and toxicity are well within the level of the ordinary skilled artisan and commonly practiced in the state of the art, and thus absent evidence to the contrary.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JEAN CORNET whose telephone number is (571)270-7669. The examiner can normally be reached on Monday-Thursday 7.00am-5.30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/JC/

/Timothy P Thomas/

Examiner, Art Unit 1628